A Low Insulinemic Diet and Lifestyle for the Primary Prevention of Aggressive Prostate Cancer with PTEN Loss

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Background
Prostate cancer with PTEN loss is a molecular subtype associated with more aggressive disease. PTEN loss enhances insulin and insulin-like growth factor signaling through the PTEN/PI3K/Akt pathway. A high insulinemic diet and lifestyle may be a milieu particularly conducive to tumors with PTEN loss. This study examines a low-insulinemic diet and lifestyle for primary prevention of prostate cancer with PTEN loss.

Methods
A prospective cohort from the Health Professionals Follow-up Study was followed for incident prostate cancer from 1986 to 2013. Participants with prevalent prostate cancer, missing baseline dietary data, or lack of follow-up after the baseline questionnaire were excluded, resulting in a final cohort of 44,036 men. Diet (every 4 years) and lifestyle (biennially) were collected via validated questionnaires. The insulinemic potential of diet was evaluated with the empirical dietary index for hyperinsulinemia (Tabung et al. Br J Nutr 2016), a score derived from 18 food groups that predict C-peptide. Diet scores were adjusted for total energy intake using the residual method. The empirical lifestyle index for hyperinsulinemia was based on the combined effect of diet, BMI , and physical activity. PTEN status was determined by a genetically validated immunohistochemistry assay on tumor tissue microarrays. Cause-specific Cox proportional hazards models including a 4-year lag for exposure and covariates were used to estimate hazard ratios and 95% confidence intervals for the competing subtypes of prostate cancer; PTEN loss and PTEN-intact prostate cancer. Confounders included diabetes history, smoking, prostate specific antigen-screening intensity and models for diet were additionally adjusted for body mass index (BMI) at age 21 and physical activity. We used inverse probability weighting (IPW) to account for the fact that PTEN status was not known for all prostate cancer cases in this cohort.

Results
Over 26 years of follow-up, 859 incident cases of prostate cancer with known PTEN status were confirmed: 142 (17%) with PTEN loss and 717 (83%) with intact PTEN. No strong association between the insulinemic potential of diet and lifestyle and the incidence of prostate cancer with PTEN loss was evident but there was a suggestion that a low insulinemic diet prevented prostate cancer with intact PTEN (**Figure 1**).

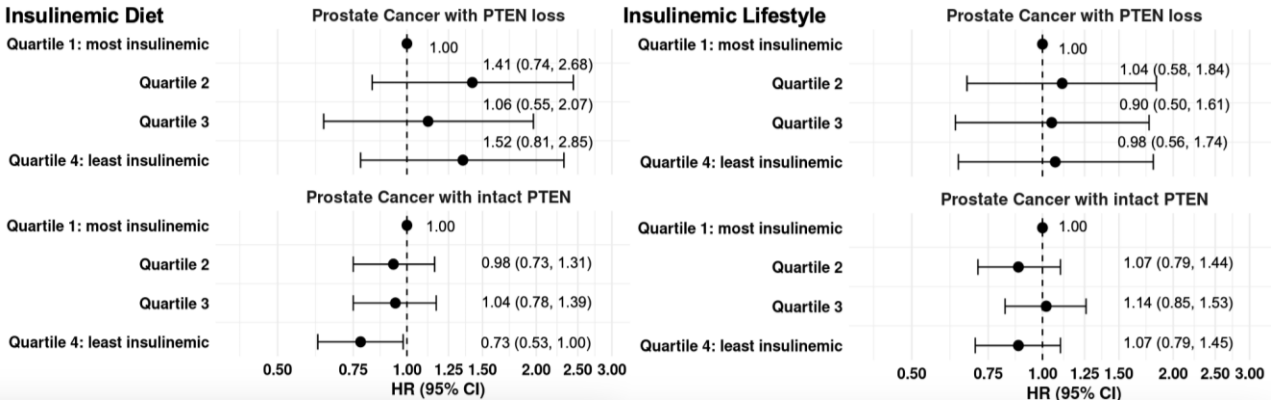

Figure 1. Insulinemic diet and lifestyle and incidence of prostate cancer by PTEN status.

Conclusions

We did not find strong evidence that a low insulinemic diet or lifestyle was protective for the primary prevention of prostate cancer with PTEN loss. We will further investigate to what extent a low insulinemic diet and lifestyle could improve survival after a diagnosis of prostate cancer with PTEN loss.

Funding Acknowledgements

This work was supported by the NCI (R37 CA275914). Tumor tissue microarrays were created at the Dana-Farber/Harvard Cancer Center Tissue Microarray Core Facility (P30 CA006516). The Health Professionals Follow-up Study was supported by the NCI (U01 CA167552). The research was also supported by a Cancer Center Support Grant (P30 CA008748). S. Flanagan, S.P. Finn, T.L. Lotan, L.A. Mucci, and K.H. Stopsack are Prostate Cancer Foundation Young Investigators.

Conflicts of Interest Disclosure Statement

S.P. Finn reports personal fees and nonfinancial support from AstraZeneca, Pfizer, and Roche and personal fees from J&J outside the submitted work. T.L. Lotan reports personal fees from AstraZeneca and grants from AIRA Matrix, Artera, and MDxHealth/Exact Biosciences outside the submitted work. L.A. Mucci reports grants from the NCI and the Prostate Cancer Foundation during the conduct of the study as well as other support from Convergent Therapeutics and grants from AstraZeneca outside the submitted work. No disclosures were reported by the other authors.